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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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FULBRIGHT & JAWORSKI, LLP
666 FIFTH AVE
NEW YORK, NY 10103-3198

EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1642	7

DATE MAILED: 09/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/270,437	CHEN ET AL.	
	Examiner	Art Unit	
	Karen A Canella	1642	

-- The MAILING DATE f this communication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *110-125,127,128,131-133,135-140,142 and 145-151* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *110, 111, 131-133, 135-140, 142148, 149* is/are allowed.

6)☐ Claim(s) *112--125, 127, 128, 145-147, 150, 151* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 108, 109, 126, 129, 130, 134, 141, 143 and 144 have been canceled. Claims 148-151 have been added. Claims 110-125, 127, 128, 131-133, 135-140, 142, 145-151 are pending and under consideration.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

3. Claims 112-117 and 124 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated vectors and isolated host cells comprising said vectors, does not reasonably provide enablement for vectors and host cells comprised within an animal or human being having been treated by gene therapy. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims..

Claims 112 and 113 are drawn to an expression vector comprising the isolated nucleic acid of claim 110 and 111, respectively, wherein said nucleic acids are operably linked to a promoter. Claims 114 and 115 are drawn to a recombinant cell comprising the expression vector of claims 112 and 113, respectively. Claims 116 and 117 are drawn to a recombinant cell comprising the isolated nucleic acids of claims 110 and 11, respectively. Claim 124 is drawn to the recombinant cell of claims 114-117 wherein said cell is a eukaryotic cell.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification states on page 19, lines 11-16 that the invention contemplates nucleic acid based therapies wherein the nucleic acids of the instant invention are incorporated into a vaccinia or adenoviral vector to render the nucleic acid transfectable into human cells. Thus, when given the broadest reasonable interpretation claims drawn to host cells and expression vectors encompass host cells and expression vectors within patient having received gene therapy or within a transgenic animal. The specification is not enabling for these uses for the following reasons:

The instant specification does not teach how to overcome problems with in vivo delivery and expression with respect to the administration of the claimed nucleic acids or viral vectors comprising said nucleic acids. The state of the art as of the priority date sought for the instant application is that in vivo gene delivery is not well developed and is highly unpredictable. For instance Verma et al (Nature, 1997, Vol. 389, pp. 239-242) teach that the Achilles heel of gene therapy is gene delivery. Verma et al state that the ongoing problem is the inability to deliver genes efficiently and to obtain sustained expression (page 239, column 3). Eck et al (Gene-Based Therapy, In: The Pharmacological Basis of Therapeutics, Goodman and Gilman, Ed.s, 1996, pp. 77-101) teach that the fate of the DNA vector itself with regard to the volume of distribution, rate of clearance into tissues etc., the in vivo consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA the level of mRNA produced, the stability of the mRNA produced in vivo, the amount and stability of the protein produced and the proteins compartmentalization or secretory fate within the cell are primary considerations regarding effective therapy. Eck et al state that these factors differ dramatically on the vector used, the protein being produced, and the disease being treated (Eck et al bridging pages 81-82).

As of the priority date sought, it was well known in the art how to infect or transfect cells in vitro or ex vivo with viral vectors. However, using viral vectors to deliver DNA to an organism in vivo, or using infected or transfected cells to deliver nucleic acids which encode a particular protein sequence to an organism in vivo is in the realm of gene therapy, and as of the priority date sought, highly unpredictable in view of the complexity of in vivo systems. Orkin et al state ("Report and Recommendation of the Panel to Assess the NIH Investment in Research on Gene Therapy", NIH, 1995) that clinical efficacy had not been definitively demonstrated with any gene therapy protocol (page 1, second paragraph). Orkin et al defines gene therapy as the transfer of DNA into recipient cells either ex vivo or in vivo (page 7, under the heading "Gene transfer"), thus encompassing the instant claims drawn to the administration of antigen presenting cells transfected or infected ex vivo. Orkin et al concludes that, "none of the available vector systems is entirely satisfactory, and many f the perceived advantages of vector systems have not been experimentally validated. Until progress is made in thee areas, slow and erratic

success in applying gene transfer methods to patients can be expected" Orkin et al comment that direct administration of DNA or DNA in liposomes is not well developed and hindered by the low efficiency of gene transfer (page 8, paragraph 5). Orkin et al teach that adequate expression of the transferred genes is essential for therapy, but that in 1995 current data regarding the level and consistency of expression of transferred genes in animal models was unknown. Orkin et al states that in protocols not involving ex vivo infections/transfection, it is necessary to target the expression of the transferred genes to the appropriate tissue or cell type by means of regulatory sequences in gene transfer vectors. The specification does not teach a vector having a specific regulatory sequence which would direct the expression of the nucleic acids within the appropriate tissue type.

The specification does not remedy any of the deficiencies or the prior art with regard to gene therapy. Given the lack of any guidance from the specification on any of the above issues pointed out by Verma or Eck or Orkin. One of skill in the art would be subject to undue experimentation without reasonable expectation of success in order to practice the methods of claims. Amendment of claims 112-117 and 124 to be qualified by the term "isolated" will overcome this rejection.

4. Claims 118-123, 125, 127, 128 and 145-147 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 118-121 are drawn to the recombinant cells of claims 114-117, respectively, wherein the recombinant cell further comprises an expression vector which contains a nucleic acid molecule encoding a cytokine which is operably linked to a promoter. Claim 127 is drawn to an expression vector comprising a mutated or attenuated virus and the isolated nucleic acid of claim 110-111. Claim 128 is drawn to an expression system useful in making a recombinant cell, comprising a first vector which encodes the protein encoded by the isolated nucleic acid molecules of claim 110 or 111, and a second vector which either encodes an MHC or an HLA molecule or an interleukin. Claim 145 is drawn to a composition useful in treating a subject afflicted with cancer comprising the recombinant cell of claim 125 and a pharmaceutically

acceptable adjuvant. Claim 146 embodies the composition of claim 145 wherein said recombinant cell expressed an HLA or MHC molecule. Claim 147 embodied the composition of claim 145 wherein said recombinant cell is a human cell. For the reasons stated above, the specification in not enabling for the use of the disclosed expression vectors and host cells for nucleic acid based therapies, wherein the expression vectors or host cell comprising said expression vectors are administered to patients having a therapeutic need for the protein expressed thereby. The specification teaches that the SEQ ID NO:5 and 7 are shorter and longer versions, respectively, of the KOC-2 gene and SEQ ID NO:6 and 8 are shorter and longer versions of the KOC-3 gene (page 12, lines 4-18). The specification teaches that both KOC-2 and KOC-3 are overexpressed in melanoma cells (page 14, lines 5-11). The specification is enabling for the isolated nucleic acids encoding KOC-2 and KOC-3 for use in diagnostic assays and expression vectors and host cells for obtaining recombinant protein for making antibodies for use in diagnostic assays. However, the specification does not contemplate a use for vectors, expression systems or host cells comprising the KOC isolated nucleic acids in combination with nucleic acids encoding cytokines, interleukins, MHC or HLA molecules, which would not be part of a therapeutic nucleic acid therapy. Further, it is noted that the recombinant cell of claim 123 cannot be used to proliferate the host cell in culture, as said recombinant cell has been rendered non-proliferate, thus the cell can only be used to deliver the disclosed nucleic acids in vivo. It is also noted that claim 127, having the specific limitation of "attenuated" viral vector has no enablement for a use in vitro as the purpose of the attenuation is to alter the virility of the virus in vivo (Brock, Biology of Microorganisms, 1979, page 547, lines 31-35). Thus, for the reasons set forth above, without further guidance from the specification, one of skill in the art would be subject to undue experimentation without reasonable expectation of success in order to practice the claimed invention.

5. Claim 127 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 127 is drawn in part to an expression vector comprising a mutated virus and the isolated nucleic acids of claims 110 or 111. The specification and claims as filed contemplate attenuated viruses, but a "mutated" virus is broader in scope than an attenuated virus as it can encompass viruses with pathogenic and other characteristics which are not part of the original characteristics of the virus. Accordingly, the contemplation of an attenuated virus does not provide adequate support for a mutated virus. This is a new matter rejection.

6. Claims 112-125, 127, 128 and 145-147 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. For the reasons stated in the rejections under 112, first above, without the limitation of "isolated expression vector" or "isolated host cell" the claims can be construed as reading on expression vectors and host cells within a patient having undergone gene therapy. Amendment of the claims to incorporate the limitation of "isolated" will overcome this rejection.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 150 and 151 are rejected under 35 U.S.C. 102(e) as being anticipated by Ross (US 6,255,055, priority to March 9, 1998).

Claim 150 is drawn to a composition comprising an expression vector wherein said expression vector encodes one or more peptide wherein each of said peptides consists of 8 to 25 consecutive amino acids of a protein .encoded by the nucleic acid of claim 110 and a pharmaceutically acceptable carrier. Claim 151 embodies the composition of claim 150, wherein said expression vector encodes a plurality of peptides.

Ross disclose an the nucleic acid encoding CRD-BP of SEQ ID NO:2 (column 6, lines 50-52). Column 4, lines 16-17 and lines 32-33 of '055 indicate that the CRD-BD protein was recombinantly expressed. The CRD-BP protein has significant sequence similarity to the proteins encoded by the instant SEQ ID NO:5, 6, 7 and 8. Alignments of the CRD-BP protein over the translation of SEQ ID NO:5-8 are provided as an attachment to this action. When given the broadest reasonable interpretation, claim 150 reads on the expression vector of Ross et al because the CRD-BP protein is a plurality of peptides consisting of 8 to 25 consecutive amino acids of the SEQ ID NO:5-8 sequences.

9. All other rejections and objections as set forth in Paper No. 18 are withdrawn.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella

Karen A. Canella, Ph.D.
Patent Examiner, Group 1642
8/26/03